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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,094	10/21/2004	Mauro Marzi	2818-224	8572
23117	7590	07/17/2006	EXAMINER	
NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203			AULAKH, CHARANJIT	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/512,094	Applicant(s) MARZI ET AL.	
	Examiner Charanjit S. Aulakh	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8, 10 and 14-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-6, 8, 10 and 14-18 is/are rejected.
- 7) ☒ Claim(s) 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. According to paper filed on April 5, 2006, the applicants have canceled claims 7, 9 and 11-13; amended claims 1-6, 8 and 10 and furthermore, have added new claims 14-18.
2. Claims 1-6, 8, 10 and 14-18 are now pending in the application.

Response to Arguments

3. Applicant's arguments filed on April 5, 2006 have been fully considered but they are not persuasive regarding enablement rejection of claims 15, 16 and 18; indefiniteness rejection of claims 15 and 18 and obviousness rejection. The applicants have amended claims to overcome prior art rejection and most of the other indefiniteness rejections. In regard to enablement rejection, the examiner does not agree with the applicants arguments that the cited references, EP 1 044 977 and US 6,242,457 teach wide spectrum of antitumor activity of camptothecin derivatives as well as activity of camptothecins in treating viral and parasitic infections (WO'876) and therefore, the instant specification is enabling for treating every known tumor, parasitic and viral infections with the instant compounds based on their topoisomerase I inhibitory activity. Contrary to applicant's assertion, Penco (US 6,242,457) teaches problems connected with the use of camptothecin derivatives as antitumor drugs such as resistance of some tumor cell lines against topoisomerase I inhibitors (see col. 3, lines 59-67). Therefore, in view of this, one can not generalize that topoisomerase I inhibitors will be effective against every known tumor cell line, every known viral or parasitic infection. As stated clearly in the last office action, it would require undue experimentation to demonstrate

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the effectiveness of instant compounds in known in vitro or in vivo models of all known tumors, parasitic and viral infections and hence their utility for treating these disease conditions.

In regard to indefiniteness rejections of instant claims 15 and 18, although applicants did not specifically address this rejection in their response, yet the examiner believes that the terms ---tumors, parasitic or viral infections--- are indefinite.

In regard to obviousness rejection, the examiner does not agree with the applicants arguments that Matsumoto reference enables only dipeptide derivative and is not predictable for camptothecin derivative. As stated clearly in the last office action, this reference leaves no doubt regarding general applicability of this approach for preparing prodrugs of compounds with low water solubility. The structure of the compound is not critical as long the compound has hydroxyl group since Matsumoto teaches functionalizing hydroxyl group with spontaneously cleavable linker strategy. The instant camptothecin compounds have a hydroxyl group present at 20th position and therefore, in order to enhance water solubility of camptothecin derivatives disclosed by penco, one skilled in the art would have been motivated to prepare the instant esters of camptothecin derivatives by functionalizing hydroxyl group with spontaneously cleavable linker strategy taught by matsumoto.

Conclusion

4. Rejection of claims 15, 16 and 18 under 35 U.S.C. 112, first paragraph is maintained for the reasons of record.

5. Rejection of claims 15 and 18 under 35 U.S.C. 112, second paragraph is maintained for the reasons of record.

6. Rejection of claims 1,2, 4, 6, 8, 10 and 14-18 under 35 U.S.C. 103(a) is maintained for the reasons of record.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 4 recites the limitation "H for variable R1" in claim 1. There is insufficient antecedent basis for this limitation in the claim. According to amended claim 1, variable R1 can not be H. However, compounds (see last two compounds on page 4 and 2nd and 3rd compounds on page 5) claimed in claim 4 recite R1 as H.

Claim 5 recites the limitation "optionally substituted with R1" in claim 1. There is insufficient antecedent basis for this limitation in the claim. According to amended claim 1, variable R1 can not be H and camptothecin derivative of formula (I) in claim 1 is always substituted with variable R1.

Claim 6 recites the limitation "optionally substituted with R1" in claim 1. There is insufficient antecedent basis for this limitation in the claim. According to amended claim 1, variable R1 can not be H and camptothecin derivative of formula (I) in claim 1 is always substituted with variable R1.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

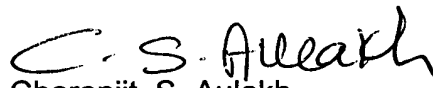
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Charanjit S. Aulakh
Primary Examiner
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